# The Ciliogenic Protein Ofd1 Regulates the Neuronal Differentiation of Embryonic Stem Cells.

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**Public Summary:**
This work modeled a human disease in embryonic stem cells and discovered that the disease gene, Ofd1, affects neuron formation.

**Scientific Abstract:**
Oral-Facial-Digital 1 (OFD1) Syndrome is an X-linked developmental disorder caused by mutations in the gene Ofd1. OFD1 syndrome involves malformation of the face, oral cavity, and digits and may be characterized by cystic kidneys and mental retardation. Deletion or missense mutations in Ofd1 also result in loss of primary cilia, a microtubule-based cellular projection that mediates multiple signaling pathways. Ofd1 mutant mice display pleiotropic developmental phenotypes, including neural, skeletal, and cardiac defects. To address how loss of Ofd1 and loss of primary cilia affect early differentiation decisions, we analyzed embryoid bodies (EBs) derived from Ofd1 mutant embryonic stem (ES) cells. Ofd1 mutant EBs do not form primary cilia and display defects in Hedgehog and Wnt signaling. Additionally, we show that ES cells lacking Ofd1 display an increased capacity to differentiate into neurons. Nevertheless, neurons derived from Ofd1 mutant ES cells fail to differentiate into V3 interneurons, a cell type dependent on ciliary function and Hedgehog signaling. Thus, loss of Ofd1 affects ES cell interpretation of developmental cues and reveals that EBs model some aspects of ciliopathies, providing insights into the developmental origins of OFD1 syndrome and functions of cilia.